Remarks

In response to the restriction requirement set forth in the Office Action mailed December 23, 2008, Applicant hereby provisionally elects Group II (claims 17-25) for continued examination, with traverse.

The Examiner imposed a ten-way restriction requirement (roman numeral IX appears to have been inadvertently skipped in enumerating the groups on page 2 of the Office Action). In support, the Examiner asserted that the inventions of Groups I-XI do not relate to a single general inventive concept. The Examiner cited 37 C.F.R. § 1.475(a)-(d) and asserted that restriction was proper because the claim groups lack the same or corresponding special technical features in being drawn to "multiple methods and multiple products." More particularly, the Examiner asserted that claims to more than one category of invention, as provided in Rule 475(b), lack unity of invention, as provided in Rule 475(c). In response, Applicant submits that the Examiner erred as a matter of law in basing the requirement for restriction on the assertion that the claims were drawn to multiple methods and products. Rule 475(b), quoted by the Examiner at page 3 of the Office Action, provides that claims to different categories of patentable subject matter will exhibit unity of invention if any one of five enumerated relationships exists between or among those claims, i.e.,

> (1) a product and a process specially adapted for the manufacture of said product; (2) a product and process of use of said product; (3) a product, a process specially adapted for the manufacture of the said product, and a use of the said product; (4) a process and an apparatus or means specifically designed for carrying out the said process; or (5) a product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

The Examiner then relied on Rule 475(c), which provides that if an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b) [of Rule 475], unity of invention might not be present. The Examiner then concluded that there is no special technical feature and restriction is proper because "there is no unity of invention or inventive step." Office Action at page 4.

As an initial matter, Applicant requests clarification of the unsupported assertion that there is no inventive step. No claim was rejected under 35 U.S.C. § 103(a) in the Office Action, and Applicant suspects that the statement was made in error.

Turning to the basis for restricting the claims into ten groups, Applicant submits that the Examiner has failed to establish a *prima facie* basis for restricting any claims in the present application because the Examiner has not characterized any pair of claims as related in any of the ways enumerated in 37 C.F.R. § 1.475(b). Thus, the Examiner has not established a basis for asserting that the claims are categorized in more or less than one of the combinations of categories of invention as specified in Rule 475(b). As a consequence, there is no proper basis for relying on the provision of Rule 475(c), which states that unity of invention might not be present if the claims fall into more or less than one of the above-quoted combinations of categories specified in Rule 475(b). For this reason alone, a *prima facie* basis for restricting the claims has not been established and, thus, the restriction requirement for asserted lack of unity of invention should be withdrawn.

Beyond the preceding dispositive issue, Rule 475(c) expressly states that "[i]f an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b) of this section, unity of invention might not be present." Rule 475(d) provides guidance as to the circumstances under which unity of invention might not be present in providing that the first recited invention in each category will be considered as the main invention in the claims and in citing to Art. 17(3)(a) PCT and 37 C.F.R. § 1.476(c). Both Art. 17 PCT and Rule 476 concern the payment of additional fees if the International Searching Authority finds a lack of unity of invention. During the international phase of prosecution of the present application, however, the International Searching Authority found unity of invention. A copy of the International Search Report establishing this fact is attached as Exhibit A. Thus, the legal basis upon which the Examiner has relied compels a conclusion that the currently pending set of claims exhibits unity of invention and the restriction requirement should be withdrawn in its entirety.

The preceding paragraphs addressed purely legal issues. Applying the law to the present facts, the issue is whether the currently pending claims are properly categorized into more or less than one combination of patentable categories specified in Rule 475(b).

Claims 17-25 of Group II were characterized as being drawn to a population of cells. Claim 17, the sole independent claim of Group II, is in product-by-process format and recites that the population of cells is prepared by introducing a DNA fragment comprising the sequence of CXCR4 into stem cells with a high amount of immature primitive progenitors. The process language of claim 17 is also the language of method claim 1, the sole independent claim of Group I, a group of claims drawn to a method of preparing or manufacturing the stem cell product of claim Group II. Thus, the claims of Group II are drawn to a product and the claims of Group II are drawn to a method specially adapted for the manufacture of that product.

Claims 26 and 28-34 of Group III were characterized as being drawn to a method for increasing the homing of stem cells. Claim 26, the sole independent claim of Group III, involves the use of the product of claim Group II (i.e., stem cells having a DNA fragment comprising the sequence of CXCR4) to repopulate a target tissue. Thus, the claims of Group III are drawn to a use of the product.

Claims 27-34 of Group IV were characterized by the Examiner as being drawn to a method for increasing repopulation of a target tissue in a subject. Claim 27, the sole independent claim of Group IV, involves the use of the product of claim Group II to repopulate a target tissue. Thus, the claims of Group IV are drawn to a use of the product.

Claim 35 of Group V was characterized as being drawn to a method of treating a disorder. By its express terms, claim 35 is dependent on any one of the claims of Group II (i.e., claims 17-25) drawn to the product. Thus, the claim of Group V is drawn to a use of the product.

Claim 36 of Group VI was characterized by the Examiner as being drawn to a method for preparing a population of cells. Inspection of claim 36 reveals that the cells being prepared are stem cells prepared by introducing a DNA fragment comprising the sequence of CXCR4 into stem cells, which is the product of claim Group II. Thus, claim 36 of Group VI is drawn to a use of the product.

Claim 37 of Group VII is characterized as being drawn to a population of cells comprising intact CXCR4 6H8. Claim 37 is a product-by-process claim reciting that the product is made by introducing into stem cells a DNA fragment comprising the sequence of

CXCR4. Thus, claim 37 is drawn to the product, a conclusion confirmed by a realization that the subject matter of claim 37 could have been defined in a claim dependent on product claim 17. The 6H8 epitope recited in claim 37 is another technical feature of that claim and Applicant does not reach the question of whether the 6H8 epitope is another special technical feature. The presence of the 6H8 epitope as another special technical feature does not alter the fact that the subject matter of claim 37 exhibits the special technical feature of a stem cell having a DNA fragment comprising the sequence of CXCR4, i.e., the special technical feature found in each of the currently pending claims.

Claim 38 of Group VIII is characterized as being drawn to a method for transplantation. Claim 38 defines the product being transplanted by reference to claim 37. Thus, claim 38 of Group VIII is a use of the product of Group VII, which is a use of the product of Group II.

Claim 39 of Group X (claim Group IX was skipped) was characterized as being drawn to a method of treating a disorder requiring a cell or tissue replacement. As expressly recited in claim 39, the method involves providing the product of claim 37 (Group VII) to a subject in need. Thus, claim 39 of Group X is drawn to a use of the product of Group VII, which is the product of Group II further comprising a 6H8 epitope, which does not change the fact that the product of Group VII is the product of Group II (each of the products is a stem cell having a DNA fragment comprising the sequence of CXCR4).

Claim 40 of Group XI was characterized as being drawn to a pharmaceutical composition. Claim 40 is a product-by-process claim reciting that the product is made by introducing into stem cells a DNA fragment comprising the sequence of CXCR4. Thus, claim 40, like claim 37, could have been drafted as a claim dependent on product claim 17 of Group II. The Examiner has not, and cannot, establish that the products of claim Groups II, VII and XI are patentably distinct.

The analysis described in the preceding paragraph reveals that each of the ten claim Groups is drawn to a product, a process specially adapted for the manufacture of the said product, or a use of the said product. This language, found in 37 C.F.R. § 1.475(b)(3) upon which the Examiner relied, demonstrates that each of the ten claim Groups falls within a single enumerated combination of categories under Rule 475(b). The language of 37 C.F.R.

§ 1.475(b), provided in highlighted form on page 3 of the Office Action, provides that "a national stage application . . . will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories . . . ." Because all of the pending claims in the ten Groups identified by the Examiner fall into a single combination of categories, i.e., enumerated combination (3) of Rule 475(b), there must be unity of invention throughout the entire set of 40 pending claims.

Confirmation that there is a single general inventive concept unifying all 40 claims is obtained by considering the special technical feature of each claim. Every pending claim includes the feature of a stem cell comprising a DNA fragment comprising the sequence of CXCR4. The Examiner has not established that the identified feature does not make a contribution over the prior art and, thus, that feature is a special technical feature. The existence of that special technical feature in each of the 40 pending claims establishes a single general inventive concept that unifies all 40 pending claims. Further confirmation that all of the pending claims exhibit unity of invention is available from inspection of the International Search Report, attached as Exhibit A, which reveals that the International Searching Authority found unity of invention for the 40 originally filed claims, which differed from the currently pending claims only in that original Swiss-type use claims (original claims 26-34 and 38) were amended to method claims in the present application.

Conclusion

For all of the foregoing reasons, Applicant submits that the restriction requirement should be withdrawn in its entirety.

Dated: January 22, 2009

Respectfully submitted,

By 

William K. Merkel
Registration No.: 40,725
MARSHALL, GERSTEIN & BORUN LLP
233 S. Wacker Drive, Suite 6300
Sears Tower
Chicago, Illinois 60606-6357
(312) 474-6300
Attorney for Applicant

Exhibit A

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(71) Applicant *(for all designated States except US)*: **YEDA RESEARCH & DEVELOPMENT CO. LTD.** [IL/IL]; Weizmann Institute of Science, P.O.Box 95, 76100 Rehovot (IL).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **LAPIDOT, Tsvee** [IL/IL]; 6 Boxer St., IL-74046 Ness-Ziona (IL). **KAHN, Joy** [IL/IL]; Bet-Shemesh (IL).

(74) Agent: **EINAV, Henry**; Inter-Lab Ltd., Science-Based Industrial Park, Kiryat Weizmann, IL-76110 Ness-Ziona (IL).

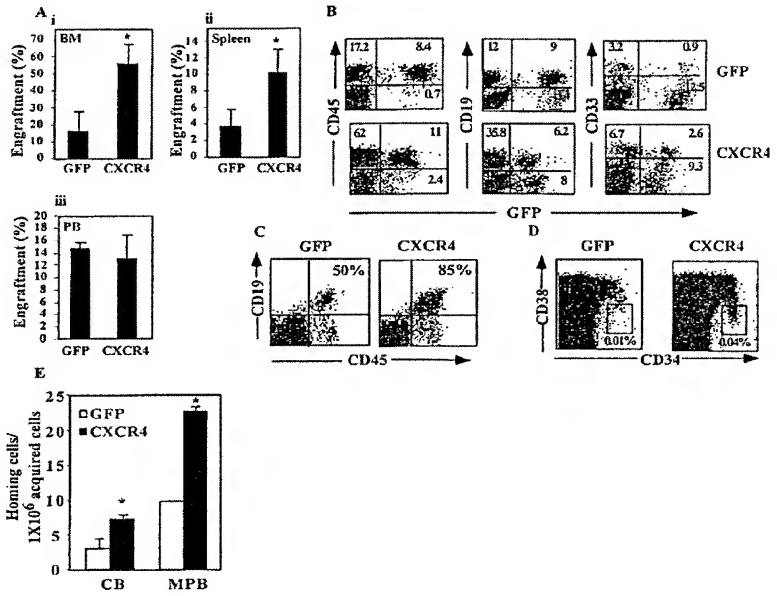
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

[Continued on next page]

(54) Title: HAEMATOPOIETIC STEM CELLS SUITABLE FOR TRANSPLANTATION, THEIR PREPARATION AND PHARMACEUTICAL COMPOSITIONS COMPRISING THEM



(57) Abstract: The present invention relates to stem cells suitable for transplantation and to methods for their preparation.

WO 2005/047494 A3

(88) Date of publication of the international search report:
23 June 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

International Application No
. . Γ/IL2004/001018

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N5/06 C07K14/715 A61K35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, PAJ, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SAWADA S ET AL: "DISTURBED CD4+ T CELL HOMEOSTASIS AND IN VITRO HIV-1 SUSCEPTIBILITY IN TRANSGENIC MICE EXPRESSING T CELL LINE-TROPIC HIV-1 RECEPTORS" JOURNAL OF EXPERIMENTAL MEDICINE, TOKYO, JP, vol. 187, no. 9, 4 May 1998 (1998-05-04), pages 1439-1449, XP000866065 ISSN: 0022-1007 figure 6	17-25,37

-/--

[X] Further documents are listed in the continuation of box C.

[ ] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
15 April 2005	04/05/2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Nichogiannopoulou, A

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Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International Application No
[illegible]/IL2004/001018

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	LOUACHE FAWZIA ET AL: "Expression of CD4 by human hematopoietic progenitors" BLOOD, vol. 84, no. 10, 1994, pages 3344-3355, XP002324832 ISSN: 0006-4971 abstract	17-25,37
P,X	KAHN JOY ET AL: "Overexpression of CXCR4 on human CD34+ progenitors increases their proliferation, migration, and NOD/SCID repopulation" BLOOD, vol. 103, no. 8, 15 April 2004 (2004-04-15), pages 2942-2949, XP002324814 ISSN: 0006-4971 the whole document	1-40
A	KOLLET ORIT ET AL: "Human CD34+CXCR4- sorted cells harbor intracellular CXCR4, which can be functionally expressed and provide NOD/SCID repopulation" BLOOD, vol. 100, no. 8, 15 October 2002 (2002-10-15), pages 2778-2786, XP002324815 ISSN: 0006-4971 the whole document	1
A	LAPIDOT T ET AL: "The essential roles of the chemokine SDF-1 and its receptor CXCR4 in human stem cell homing and repopulation of transplanted immune-deficient NOD/SCID and NOD/SCID/B2mnull mice" LEUKEMIA (BASINGSTOKE), vol. 16, no. 10, October 2002 (2002-10), pages 1992-2003, XP002324816 ISSN: 0887-6924 page 1998, right-hand column, line 1 - page 1999, left-hand column, line 31	1

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL2004/001018

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 7, 29-36 and 39 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [X] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claims 7, 29-36 and 39 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box II.2

Present claims 1-40 relate to stem cells in general, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only human hematopoietic stem cells (HSCs). In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the effect of CXCR4 overexpression on human HSCs.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.